SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Cellular and Molecular Immunology

has the honor to invite you to the public defense of the PhD thesis of

Helena Van Damme

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:
Identification and validation of biomarkers for immunoregulatory cell populations in the tumor microenvironment

Promotors:
Prof. dr. ir. Jo Van Ginderachter
Prof. dr. ir. Damya Laoui

The defense will take place on
Wednesday, December 15, 2021 at 14h30

The defense can be followed through a live stream. Contact Helena.Van.Damme@vub.be for more information

Members of the jury

Prof. dr. Joske Ruytinx (VUB, chair)
Dr. Els Pardon (VUB, secretary)
Prof. dr. Nick Devoogdt (VUB)
Prof. dr. Luc Leyns (VUB)
Prof. dr. Adrian Liston (Babraham Institute, UK)
Dr. Fabienne Andris (ULB)

Curriculum vitae

Helena Van Damme obtained the degree of Master of Science in Biology with greatest distinction at the VUB in 2016. Afterwards she started as a PhD student at the lab of Cellular and Molecular Immunology under the promotorship of Prof. Jo Van Ginderachter and Prof. Damya Laoui.

During her PhD she studied the intra-tumoral heterogeneity of immune cells and aimed to identify and validate potential biomarkers for the pro-tumoral cell populations.

Abstract of the PhD research

While **cancer immunotherapy** has significantly advanced in the past few years, there is only a minority of patients with advanced disease who show durable responses. This lack of success is due to the complex and highly regulated nature of the immune system. Indeed, there are multiple immunological steps that need to be fulfilled in order to ensure successful elimination of the cancer cells. This multi-step complexity indicates the need for the development of **combination therapies**, which modulate different aspects of the anti-tumor immune response.

In this PhD, we aimed to identify universal biomarkers for immunoregulatory cell populations in the tumor microenvironment. In this respect, we were able to discern **a protumoral Treg population** in both mouse and human tumors which was marked by its unique expression of the CCR8 chemokine receptor. We generated **CCR8-specific immunotherapeutic compounds** that enabled the selective depletion of CCR8-expressing ti-Tregs from the tumor. This ti-Treg depletion elicited **antitumor immunity** and reduced tumor growth **when combined with another immunotherapeutic compound**. These results indicate that CCR8-targeting can be a powerful addition to current immunotherapeutic strategies.

Aside from the distinct ti-Treg populations, we also identified **distinct subsets of tumor-associated macrophages (TAMs)**. The most **anti-inflammatory** of these macrophages were characterized by a uniquely high expression of the **CCL8 chemokine**, which is known to interact with CCR8, among other receptors. This transcriptional macrophage phenotype could also be identified in human non-small cell lung cancer (NSCLC) tumors, indicating the **conserved** nature of this immune subset between mouse and **human**.

Altogether, this PhD work has contributed to the identification and validation of distinct biomarkers (CCR8/CCL8) on immunoregulatory cells within the tumor microenvironment. Findings in mice readily translated to findings in human patients. Moreover, this work also provides preclinical proof of concept for the use of CCR8 as a therapeutic target in combination therapies.